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Poststroke alterations in heart rate variability during orthostatic challenge

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Abstract

Older adults following recovery from ischemic stroke have a higher incidence of orthostatic hypotension, syncope, and fall risk, which may be related to impaired autonomic responses limiting the ability to maintain cerebral blood flow. Thus, we investigated cerebrovascular and cardiovascular regulation in 23 adults ≥55 years of age, 10 diagnosed with ischemic stroke, and 13 age-matched healthy controls when sitting at rest and upon standing to compare differences of autonomic variables at ~7 months (218 ± 41 days) poststroke.

Arterial blood pressure via finger plethysmography, muscle-pump baroreflex via electromyography, heart rate variability via 3-lead ECG, and cerebral blood flow velocity via transcranial Doppler were analyzed while sitting for 5 minutes and then during quiet standing for 5 minutes.

From the seated to standing position, the stroke group had significantly greater decline in the low frequency component of heart rate variability (164 [79] vs 25 [162] ms^2; $P = 0.043$). All other cardiovascular parameters and assessments of autonomic function were not significantly different between the two groups.

Our findings support the hypothesis of continued autonomic dysfunction after recovery from ischemic stroke, with potential attenuation of the cardiovascular response to standing. However, further investigation is required to determine the mechanisms underlying the increased risk of orthostatic hypotension, syncope, and falls poststroke.

Abbreviations: ANS = autonomic nervous system, EMG = electromyography, FFT = fast Fourier transform, HF = high frequency, HRV = heart rate variability, LF = low frequency, NTS = nucleus tractus solitarius, OH = orthostatic hypotension, RRI = R-to-R time interval.

Keywords: ageing, autonomic dysfunction, fall risk, heart rate variability, orthostatic challenge, orthostatic hypotension, stroke

1. Introduction

Medically treated nonfatal falls among those 65 years of age or older living in the US is currently a multibillion-dollar healthcare expenditure.[1] Ischemic stroke is a significant cause of gait imbalance and falling,[2,3] with incidence of stroke more than tripling between the 35 and 44 to 65 and 73-year-old age groups.[4,5] Autonomic dysfunction has proven to be both a risk factor and also as a symptom poststroke, attributing to the increased fall risk in stroke survivors.[3,5–7]

Regulation of blood pressure and heart rate involves fast, neurally mediated reflex systems. The central autonomic network, which includes the nucleus tractus solitarius (NTS) and ventrolateral medulla, in conjunction with the cardiac, carotid, and aortic arch baroreceptors of the peripheral nervous system are involved in those systems. The pathophysiology underlying autonomic dysfunction following both ischemic and hemorrhagic stroke involving these structures remains elusive due to the complexity of contributing factors such as comorbidities and location of ictus.[8,9] Nonetheless, many studies have attributed an increase in cardiovascular and all-cause mortality to the alterations in autonomic control poststroke.[8–10] Decreased cardiac baroreceptor reflex sensitivity (BRS) and reduced vagal inhibitory outflow, both of which can be measured via noninvasive techniques such as heart rate variability (HRV), have been seen up to 9 months after ischemic stroke.[11] Poststroke increased arrhythmogenic potential, blood pressure variability, sympathetic tone, and altered cerebral perfusion all lead to a poor prognosis.[9–11]

The sum of aging, gait imbalance,[3] and muscle weakness,[12] with cardiovascular autonomic dysfunction in the elderly poststroke precipitates an exaggerated risk of orthostatic intolerance and falls, increasing morbidity, mortality, and health care costs in this population.[1,2,4–8] Thus, we utilized noninvasive techniques to perform a cross-sectional investigation of the

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degree of autonomic dysfunction in adults ≥55 years of age that are less than 1-year poststroke.

2. Methods

2.1. Study population

Twenty-three subjects (10 poststroke and 13 controls) gave written informed consent to participate in the pilot study. Approval was obtained from the Ethics Committee of the Medical University of Graz. Stroke patients 55 years of age and older were included in the study if the cerebral ischemic infarction had occurred in the 12 months prior to the study and was diagnosed by magnetic resonance imaging (MRI). Due to our testing procedure, only patients with transient or mild stroke syndromes (National Institutes of Health Stroke Scale [NIHSS] ≤3) were selected. Stroke patients with further neurological disorder (epilepsy, dementia, and Parkinson's disease), severe disability (modified Rankin scale [mRS] >2), and/or intracranial vessel stenosis were excluded. The control group consisted of age-matched subjects with no history of stroke that fulfilled the inclusion criteria previously described. Total vascular risk for each subject was calculated by adding each individual risk factor (eg, previous vascular event, tobacco use, arterial hypertension, dyslipidemia, and diabetes mellitus), which were obtained from reviewing history and medical records. All subjects underwent basic neurological assessment (clinical neurological examination; extra- and intracranial duplex sonography) and received medical clearance to participate prior to performing a single sit-to-stand test at the Neurological Department of the Primary and Tertiary Care University Hospital of Graz.

2.2. Equipment used and measurements performed

Cerebral blood flow velocity (BFV) of the middle cerebral artery was measured using a transcranial Doppler (TCD) (Multi-Dop T digital, Compumedics Germany GmbH, Singen, Germany). Arterial blood pressure was measured with noninvasive finger plethysmography (Finometer, Finapres Medical Systems B.V., Amsterdam, Netherlands), and the heart rate (HR) was measured using bipolar 3 lead ECG (FD-13, Fukuda Denshi Co. Ltd, Tokyo, Japan). Standard arterial blood pressures, derived from a continuous pressure trace acquired using a digital artery cuff placed on the middle finger with the hand held at heart level assisted with an arm sling, were obtained during sitting and standing. The force plate (AccuSway, Advanced Mechanical Technology, Inc., Watertown, MA) was zeroed before each subject placed his or her feet into position. To obtain muscle-pump baroreflex responses, electromyography (EMG) of bilateral gastrocnemius muscles was performed (MyoSystem 1200, Noraxon USA Inc., Scottsdale, AZ). Analog outputs were digitized using an USB-6218 integrator (National Instruments Corporation Ltd., Newbury, UK) and recorded on LabVIEW 13.0.1f2 (National Instruments Corporation Ltd., Newbury, UK).

2.3. Experimental protocol

Following 5 minutes of sitting at rest on a bed adjusted to patient knee height (sitting), subjects were gently assisted into the standing position (standing) on a force plate while looking straight ahead. After 5 minutes of quiet standing, the subject was assisted to resume the initial seated position (recovery) for a further 3 minutes. Subjects were instructed to breathe naturally throughout the protocol and when standing, to sway or shift their weight if they felt uncomfortable, but asked to stay as still and relaxed as possible, with their shoes off and feet shoulder width apart on a force plate. Medical personnel and an open bed nearby were available should a subject become syncopal. All investigations were performed between 7:00 and 11:00 AM inside a quiet room maintained at 23 to 25 °C. Subjects were asked to refrain from coffee or other stimulants for 24 hours prior to study participation.

2.4. Data extraction

Sampling rate for output data was 1 kHz. R-to-R time interval (RRI) was measured using peak detection software accurate to 1-ms. ECG data were screened manually for artifacts such as premature ventricular contractions, HR was derived from the average RRI of each epoch in addition to RR interval standard deviation (RRSD) standardized to 15 seconds for each subject per epoch. Spontaneous baroreflex response was determined from changes in RRI and systolic blood pressure (SBP) described by Blaber et al.[13,14]

HRV was derived via the fast Fourier transform (FFT) method, following RRI detection (MATLAB, Mathworks, MA). FFT was performed on 260-second sections from each of the 3 protocol epochs using Welch method (64 seconds Hanning window with 50% overlap) to determine the absolute (milliseconds^2) and normalized (Equation 1) very low frequency (VLF: ≤0.04 Hz), low frequency (LF: 0.04–0.15 Hz), and high frequency (HF: 0.15–0.4 Hz) power density.[15]

$$((\mathrm{LF} \text{ or } \mathrm{HF})/(\mathrm{Total\,Power} - \mathrm{VLF}))^{*}100$$

Equation 1: HRV normalization

The EMG data were rectified and low pass filtered (cutoff frequency 5 Hz) to extract the envelope using the moving average method. Beat to beat EMG impulses (ie, area under the EMG envelope during each RR interval) were then calculated to represent the overall effect of EMG within each beat. The muscle-pump baroreflex sensitivity was characterized by the transfer function gain[16] from SBP to EMG impulse series in 3 frequency bands (VLF: 0.01–0.07 Hz; LF: 0.07–0.15 Hz; and HF: 0.15–0.3 Hz).[17] The transfer function was estimated by Welch method (64 seconds Hanning window with 50% overlap) from SBP and EMG impulse during the 5-minute standing period. The gain value at a given frequency was considered to be valid only if the magnitude squared coherence between SBP and EMG impulse at the same frequency was greater than 0.5.

2.5. Statistical analysis

Autonomic parameters including HR, SBP, diastolic blood pressure (DBP), HRV, systolic baroreflex, lag time, and cerebral blood flow velocity (both SBFV and DBFV) are presented as median ± interquartile range (IQR) with nonparametric statistics employed to compare stroke and control groups. Nominal data (gender, use of daily antihypertensive, and total vascular risk factors) were compared using chi-squared test. Anthropometric data (eg, age, height, and weight), SBP nadir after standing, the time required to reach peak SBP after the nadir (overshoot), and for return to within 10 mm Hg of that acquired in the 3rd minute of standing (plateau) for 5 seconds were compared between groups via Mann–Whitney *U* testing. Average autonomic variables during 15 seconds in the 5th minute of sitting, 3rd minute after standing, and during recovery were also compared between stroke and control groups via Mann–Whitney *U* testing. Similarly, muscle-pump baroreflex gain values in the VLF band (insufficient data points in LF and HF bands due to low

Table 1

Demographics of stroke and control groups.

	Stroke (n = 10)	Control (n = 13)	*P*
Age, years	64.1 ± 7.5	62.1 ± 7.1	0.518
Male, no. (%)	9 (90)	5 (39)	0.012
Weight, kg	89.5 ± 16	82.6 ± 17	0.331
Height, cm	177 ± 6	170 ± 10	0.054
Total vascular risk factors*	2 ± 1.25	0 ± 1	0.005
Daily antihypertensive, no. (%)	7 (70)	2 (15)	0.001
Time poststroke, days	218 ± 41		
Stroke type, no.	Cardio-embolic, 4 Large vessel, 2 Cryptogenic, 4		

Values are presented as median ± interquartile range (IQR), unless otherwise mentioned.
* Total vascular risk factors calculated by the addition of risk factors (diabetes mellitus, tobacco use, hypertension, and hyperlipidemia), with each factor valued as 1 point.

coherence between SBP and EMG impulse) were compared using the Mann–Whitney *U* test. Spearman correlation between all autonomic variables and NIH stroke severity score or vascular risk factors was performed using Prism 6 (Prism 6 for Mac OSX, GraphPad Software, Inc. San Diego, CA). Statistics were performed using SPSS v23 (SPSS Statistics for Windows, IBM Corp Armonk, NY), with significance assumed at $P < 0.05$.

3. Results

The proportion of male subjects (X^2 (1, N = 23) = 6.3, $P < 0.05$), those taking daily antihypertensive medication (X^2 (1, N = 23) = 11.6, $P < 0.01$), and total vascular risk factors (X^2 (3, N = 23) = 12.3, $P < 0.01$) were significantly greater in the stroke group. There was no difference in age, height, or weight between the stroke and control subjects (Table 1).

Poststroke subjects demonstrated a significantly greater decline in the LF power spectra (164 [79] vs 25 [162] ms^2; $P = 0.043$) when standing from a sitting position (Table 2). No significant differences between group averages for heart rate, blood pressure, cerebral blood flow velocity, spontaneous baroreflex, baroreflex lag time, and blood pressure response time (overshoot and plateau) were observed between the stroke and control group at any position (Table 3). HRV did not differ significantly

Table 3

Median (±IQR) heart rate variability indices during sitting and standing and delta between them in stroke and control groups.

HRV parameter	Position	Stroke	Control	*P*
HF, ms^2	Sitting	126 (124)	116 (171)	0.612
	Standing	76 (251)	65 (62)	0.772
	Δ	39 (141)	7.6 (126)	0.942
HF, n.u.	Sitting	0.22 (0.16)	0.31 (0.42)	0.469
	Standing	0.32 (0.43)	0.24 (0.09)	0.772
	Δ	−0.07 (0.26)	-8.1×10^{-5} (0.21)	0.247
LF, ms^2	Sitting	313 (186)	121 (222)	0.128
	Standing	128 (106)	105 (189)	0.772
	Δ	164 (79)	25 (162)	0.043
LF, n.u.	Sitting	0.78 (0.16)	0.70 (0.42)	0.469
	Standing	0.68 (0.43)	0.76 (0.09)	0.772
	Δ	0.07 (0.26)	-8.1×10^{-5} (0.21)	0.247
LF/HF	Sitting	3.53 (3.0)	2.28 (4.1)	0.469
	Standing	2.24 (4.4)	3.2 (1.5)	0.772
	Δ	0.31 (2.5)	−0.01 (2.5)	0.469

Δ = difference between sitting and standing, HF = high frequency, HRV = heart rate variability, IQR = interquartile range, LF = low frequency, n.u. = normalized units.

Table 2

Median (±IQR) autonomic variables for stroke and control groups at various time points.

Variable	Position/parameter	Stroke	Control	*P*
SBP, mm Hg	Sitting for 5 min	119 (15)	119 (22)	0.901
	Sitting to nadir diff	17 (7)	15 (20)	0.420
	Standing for 3 min	118 (21)	128 (24)	1.000
	Recovery for 3 min	114 (26)	118 (22)	0.951
DBP, mm Hg	Sitting for 5 min	71 (14)	72 (20)	0.852
	Stand to nadir diff	13 (8)	8 (11)	0.557
	Standing for 3 min	73 (10)	77 (22)	0.457
	Recovery for 3 min	72 (12)	72 (19)	0.901
SBFV, cm/s	Sitting for 5 min	53 (31)	59 (15)	0.457
	Stand to nadir diff	6 (11)	10 (28)	0.901
	Standing for 3 min	50 (30)	64 (15)	0.321
	Recovery for 3 min	51 (27)	59 (7)	0.239
DBFV, cm/s	Sitting for 5 min	18 (11)	25 (9)	0.215
	Stand to nadir diff	18 (8)	9 (27)	0.321
	Standing for 3 min	19 (12)	28 (9)	0.082
	Recovery for 3 min	19 (14)	22 (10)	0.215
Heart rate, bpm	Sitting for 5 min	69 (5)	73 (13)	0.193
	At nadir	76 (9)	83 (14)	0.063
	At plateau	76 (11)	81 (9)	0.094
	Standing for 3 min	75 (9)	79 (14)	0.321
	Recovery for 3 min	67 (7)	71 (14)	0.420
Avg. baroreflex, ms/mm Hg	Sitting for 5 min	5.7 (3.8)	5.0 (5.1)	1.000
	Standing for 3 min	4.9 (2.5)	4.0 (2.8)	0.554
Lag time, s	Sitting for 5 min	0.6 (0.1)	0.59 (0.3)	0.670
	Standing for 3 min	0.59. (0.2)	0.72 (0.3)	0.286
Blood pressure response time, s	Time to reach plateau	26.1 (13.3)	23.5 (5.7)	0.975
	Time to reach peak	9.2 (2.6)	7.1 (6.1)	0.193

Nadir represents values when the lowest SBP is observed (upon standing) and plateau at SBP stabilization (upon standing). Lag time represents the time interval between change in RR-interval following a change in SBP. IQR = interquartile range, SBFV/DBFV = systolic/diastolic blood flow velocity, SBP/DBP = systolic/diastolic blood pressure.

between the 2 groups at any position other than for the difference in LF (ms^2) from sitting to standing (Table 2). No significant correlation was found between autonomic variables and total vascular risk factors or NIH stroke severity score.

4. Discussion

The main finding of this study was a greater magnitude of decrease in LF HRV modulation for the stroke group on average compared to the control subjects.

4.1. Heart rate and HRV

The autonomic nervous system (ANS) directly influences the RRI and HRV, which both provide an indicator of sympathetic and parasympathetic autonomic modulation.[15] Power spectral analysis of variability in the RRI for short (2–5 minutes) ECG recordings can be divided into HF, LF, and very low (VLF) frequency components via the FFT method.[15] When expressed in normalized units, the HF component is considered representative of parasympathetic modulation of the RRI, while LF is a marker of sympathetic modulation, although some interpret an influence of both ANS branches on LF when expressed in absolute units.[15] Interestingly, increased lower frequency power components (eg, LF, VLF) may act as risk predictors strongly associated with mortality postmyocardial infarction.[8,18,19] Time domain methods are simple calculations such as the standard deviation of the RR interval (aka RRSD or SDNN), which, when standardized for time, represents total power or overall global HRV.[15]

We found that the spontaneous baroreflex response time and HRV via the FFT method was not significantly different between the 2 groups when orthostatically challenged, even when controlling for male gender. A larger decrease in LF upon standing, representing a transition to less sympathetic modulation, was found on average in the stroke group upon standing. This indicates a paradoxical decrease in sympathetic modulation of the heart rate during orthostatic challenge and the opposite response to that of the average healthy control (Fig. 1). Alteration in normal sympathetic modulation to physiologic stress could signify an underlying dysfunction at the level of the NTS.[10] Redistribution of modulation toward sympathetic influence in response to the decreased firing from the baroreceptors should lead to the natural physiological pattern observed in the control group. This is assuming that the sites containing baroreceptors are anatomically normal and not affected by atherosclerosis and stenosis; further ultrasound or arteriograms of the carotids could help rule out anatomic pathology. HRV derived via FFT comparisons between stroke and control groups averages did not show statistical significance, which restricts the supposition that stroke was an influential factor, but the average HR and HRV trends suggest underlying dysfunction of central ANS organization at baseline and in response to orthostatic challenge, decreasing the capacity to accelerate heart rate, in the stroke group.

Average heart rate remained slightly higher throughout the protocol in the control group, though not significant, and this could signify a greater baseline β-receptor quantity or sensitivity, which correlates with relatively larger increase in HR after orthostatic challenge (12 ± 6 vs 9 ± 8 bpm). A larger sample size and more equal distribution of demographics for both groups would be required to confirm who is better equipped to maintain cerebral perfusion in response to orthostatic challenge and would be less likely to fall due to syncope.

Two theories to explain the poststroke alteration in autonomic function include: the ischemic damage could be affecting NTS signaling, resulting in constant sympathetic activity, which over time can increase resistance at adrenergic beta-receptors to stimulation;[20] or there may be a greater inhibition of sympathetic catecholamine release. Those with hypertension, stroke, and chronic heart disease often display this type of reactivity and the results of resting heart rate being comparatively lower before and after standing for the stroke group correlates with either of these theories.[20] The exact mechanisms for these differences are still unknown, but Tang et al attributed autonomic dysfunction as the major influence in the high prevalence of orthostatic hypotension (OH) in their stroke subjects and may have been revealed with a larger study.[9]

4.2. Blood pressure

Assuming an upright position creates a gravitational gradient leading to blood accumulation in the lower body, taking away central blood volume and concomitantly cerebral blood volume.[21] Although the difference in the magnitude of SBP or

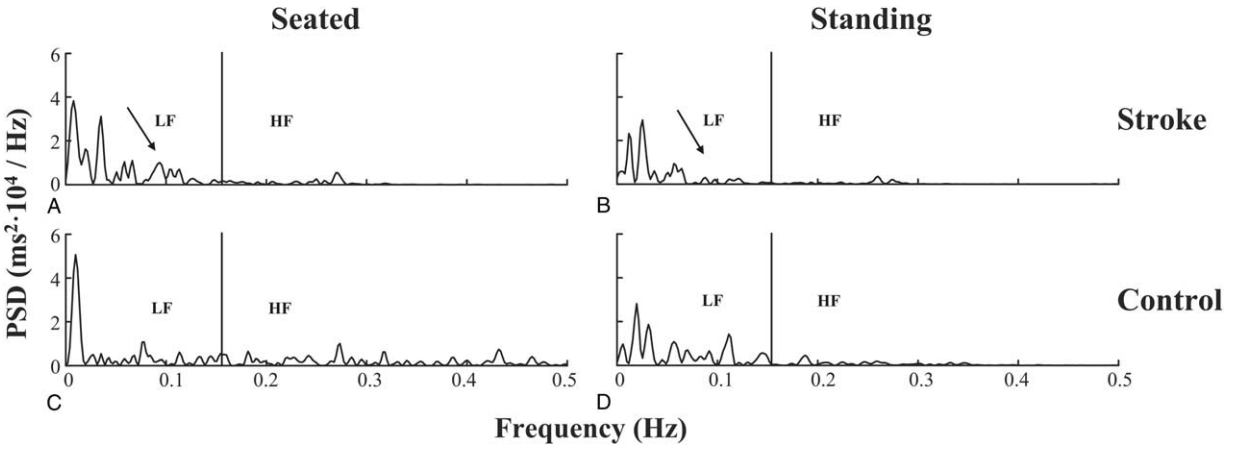

Figure 1. HRV spectra calculated by an FFT based nonparametric algorithm during seated (A, C) and during standing (B, D) for a stroke subject (A, B) and a control subject (C, D). Note the decrease in low frequency (0.04–0.15 Hz) spectra in the stroke subject after standing (black arrow). FFT = fast Fourier transform, HRV = heart rate variability, PSD = power spectral density.

DBP decreasing after standing was not statistically different between the 2 groups, it is interesting to note that the average BP drop for the stroke group in this study approached the criteria for OH.[22] Prior studies have shown that an increased risk of syncope occurs when cerebral perfusion decreases in response to a significant drop in central BP, with the mechanism being linked to withdrawal of excessive sympathetic activity.[23] The greater baseline sympathetic modulation (ie, LF values) and greater magnitude at which RRSD decreased seen in the stroke group could lead to an earlier withdrawal of sympathetic vascular tone, with an increased risk of syncope especially if beta-adrenergic responses are blunted.[9,20]

We found no significant difference in spontaneous baroreflex sensitivity between the 2 groups during standing. However, the gain values from SBP to EMG impulse were attenuated in the stroke group, which implies a poststroke impairment of muscle-pump baroreflex. This correlates with the observation that the average BP drop upon standing for the stroke group approached the criteria for OH as well as the slightly longer BP recovery time in the stroke group. An impaired muscle-pump baroreflex may be attributed to muscle atrophy after bed rest in stroke patients and/or affected nerve pathways to the muscular system. This could be further investigated by recording and analyzing motor unit activation and recruitment.

4.3. Stroke correlation

Acute ischemic stroke can occur due to various reasons including trauma, dehydration, hypercoagulation, arrhythmias, and drug exposures. More commonly, chronic disease states such as diabetes, hypertension, and vasculitides play a role in the atherosclerotic plaque formation and blood vessel damage that can lead to ischemic or hemorrhagic stroke. There is direct evidence for the effects of chronic disease states on the function of adrenergic receptors,[8,9] necessitating greater doses of synthetic or endogenous catecholamines to elicit responses, especially in shock states.[20] This may be the reason for some of the observed resistance to the sympathetic modulation in chronotropy in the group with a greater quantity of vascular risk factors. Aging could also influence this resistance, secondary to arteriosclerosis, and may be a reason why statistical differences were not so prevalent between age-matched stroke and control groups. Age is a risk factor associated with coronary heart disease in current American College of Cardiology/American Heart Association clinical screening guidelines, and we did not exclude anyone based on history of hypertension.[24] Chronic hypertension damages coronary, cerebral, and any other blood vessels, so if both the stroke and control group subjects of this study had histories of hypertension, they will both be more likely have altered blood pressure regulation and be at risk for adverse vascular events compared to healthy, younger individuals. Nevertheless, the stroke and control groups in this study did not show major differences in regulation of blood pressure and heart rate. Clarification of the mechanism behind stroke injury related autonomic dysfunction, along with screening of the associated risk factors involved in falling, is critical for the rapidly growing elderly population in need of preventative strategies.[2,3,9]

4.4. Future research

Our attempt to integrate associated cardiovascular and cerebrovascular variables into a combined analysis using numerous noninvasive methods highlights the need for improved orthostatic intolerance and fall risk screening protocols. Hand held analysis of global HRV is already available, which may streamline data collection during more realistic physiologic challenges outside of the laboratory. Approaches to testing autonomic capability by a simple mechanism that does not utilize the baroreceptor reflex (eg, oculocardiac reflex) could also help delineate between vessel disease and central autonomic dysfunction at the bedside.[11] Autonomic dysfunction after exposure to microgravity (aka postflight adaptation syndrome) is another area being investigated for mechanism clarification and novel screening techniques.[17,25,26] From a clinical standpoint, HRV has been described as a strongly associated clinical marker for mortality after myocardial infarction,[15,18] while greater blood pressure variability is associated with increased disability after stroke.[27] However, further elucidation of the relationship of HRV with isolated stroke is needed.

Rehabilitation strategies could combine mobile monitoring of the cardiovascular and autonomic systems with effective physical therapy measures to protect the elderly suffering from weakness after stroke, such as using underwater treadmills to support body weight.[28] Further evaluation of the plasma for humoral differences (eg, catecholamines, antidiuretic hormone, atrial natriuretic peptide, renin, aldosterone, adrenomedullin and galanin, etc.) between the stroke and control groups involved in this study is underway. There could also be value in a similar future sit-to-stand protocol that includes muscle sympathetic nerve activity (MSNA) evaluation, which could help distinguish the magnitude and timing of sympathetic responses seen, while clarifying the relationship between MSNA and HRV.

4.5. Limitations

First, the sample size with which we conducted this study was small. Second, differences in our sample population were noted for age and medication usage, and were significant for gender. Goswami et al[29] observed that when comparing individuals exposed to artificial gravity via a human centrifuge, women showed greater tendency for orthostatic intolerance, therefore gender could be a confounding factor in comparing our subject groups under orthostatic stress. Antihypertensive medication usage is a confounding factor, but Panayiotou et al[30] examined orthostatically challenged cardiovascular responses 1 week after a stroke and found no significant changes in parameters between patients using antihypertensive medication and those who were not. Other research groups have investigated orthostatic tolerance greater than 1-year poststroke, often finding continued ANS dysfunction.[9] Since our stroke group postinsult time interval falls between these 2 studies, we cannot assume that our subjects' responses are comparable. Last, positioning also plays a role in confounding autonomic regulation with some studies including an initial supine position into the standard sit-to-stand protocol, which could alter neurovestibular activity and subsequent cerebral autoregulation.[30,31]

5. Conclusions

This pilot study was undertaken with the intent to screen for differences in overall cardiovascular reflexes after physiological perturbation with a simple orthostatic challenge on older patients with and without a history of recent stroke. The most important finding from this study was the magnitude of HRV decrease upon standing in our stroke group. Our findings support previous studies linking abnormal central autonomic function with

alteration in neuronal organization months after cerebrovascular ischemic injury.

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